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# [illegible] GROWTH OF THE ANTIBIOTICS INDUSTRY AND SOME SUGGESTIONS FOR ANTIBIOTIC RESEARCH

Report by Yi Ching-hsiang, Vice Minister of Light Industry at the 1955 Antibiotic Conference of the Chinese Academy of Science

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Yi Ching-hsiang

The First Five-Year Plan of the Chinese People's Republic to develop the people's economy has placed the emphasis of the pharmaceutical industry on antibiotics which greatly affect the people's health, and the Chinese Academy of Science has also designated antibiotics as one of the 11 focal points of research during the 5 year period. Therefore it is both timely and important that the Academy of Science has called this conference for the interchange of technical experience, the mapping of working plans, the [illegible] of research activities, and the stimulation of production. On behalf of the Ministry of Light Industry, I welcome all [illegible] attending this conference, and rejoice [illegible] this conference.

There is no doubt that China's [illegible] great stimulation with so many specialists attending this conference. I feel very fortunate to have such a good opportunity to talk about the present status and development of China's antibiotics industry with you. I shall also point up existing important [illegible] and expect helpful direction and suggestions from you.

## I. THE PRESENT STATUS AND ACCOMPLISHMENTS OF THE ANTIBIOTICS INDUSTRY IN CHINA

The production of antibiotics and the activities of national construction are closely interrelated. The people of the whole nation await us. This is a difficult task. After the liberation, under the correct leadership of the Chinese Communist Party and the People's government, our country had already had an antibiotics industry. That combined with the toils of the scientists and the great mass of occupational workers caused the industry to develop very rapidly. After the Chinese People's Republic was formed, antibiotic research was expanded on a national scale. The Chinese Academy of Science, the various research units in the Ministry of Health, certain institutions of higher learning, and the research laboratories of the nationalized pharmaceutical industry all conducted research on the most frequently used antibiotics such as penicillin, chloramphenicol, etc. This had a great effect on the training of qualified people and the improvement of techniques. During the exploratory stages of such research activities, these scientists overcame many difficulties, continued to study and experiment to lay the first foundations, for the industrial production of antibiotics. In 1949, under the leadership of the Ministry of Health, research and experimentation on penicillin was begun. Due to the emphasis put on it by the party and the government, it was not long before formal production on an experimental basis was begun. At present, the scale of production still is not large. But research work during the few years after the liberation has rapidly resulted in the

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possibility of antibiotic manufacture on an industrial basis. There is no doubt about that.

The status of industrial production at present shows that the production of penicillin has advanced from the nonexistent stage to the existent stage. Furthermore its production capacity continues to increase each year. Roughly the 1953 quantity is 12.6 times that of 1952, that of 1954 is 43 times, and that for 1955 is calculated at 160 times (that of 1952). Fundamental research has been completed on the method to be used and the source of raw materials required for the manufacture of chloramphenical. The production of synthomycin has been initiated in June 1955. Its production in this early stage has been able to meet China's needs at the present time. The combined research efforts on aureomycin by the various units has shown sufficient result for its manufacture to be done on an experimental basis. Streptomycin is also in the research stage of experimental manufacture. This is the beginning for all of this to be coordinated into the new foundation to expand production.

The development of China's antibiotic industry is the result of continual advances in research activities and production. The following items are the more important accomplishments of technique.

1. Continual improvements have been made in the methods of penicillin production, so that fermentation units have continued to increase. The average for October this year has reached more than 2,000 units. Improvements have also been made in mold culture as some tanks that have been rotating for more than a year did not show any signs of mold growth. Cottonseed meal was used instead of cornmeal. This substitution was more in keeping with China's economic conditions, and it overcame the present difficulty that the nation cannot produce a better quality cornmeal on a large scale, the result of which advanced the production of penicillin to an earlier date. A Waldhof type of fermenter is used to cut down on the amount of air that is needed (it uses 0.5 vol air per minute). The fermenting period is reduced from 90 hours to 65 hours, and the utilization rate of the facilities is increased. From the standpoint of extraction and purification the total production rate of procaine penicillin has been raised from 60% in 1953 to roughly 75% at the present time. Furthermore the crystals of procaine penicillin are fine and small enough to meet clinical needs. Color standards set for the intermediate product and the finished product have improved the color of the finished product.

2. Synthesis of chloramphenical has met with preliminary success through the cooperative research efforts of the Chinese Academy of Science and the Northeast Pharmaceutical Plant of the Ministry of Light Industry. As problems on the separation of the optically active bodies and disintegration of the dextro-rotating bodies still need further economic and logical study, production of synthomycin is carried out at the present time. Important results in experimental production are as follows.

A. Development of a new method to manufacture p-nitroacetophenone through the oxidation of nitrobenzene using a strong neutral potassium permanganate as the oxidizing agent, with the average yield rate in the purified form being 75%.

Calculated from the benzene grouping the total rate of p-nitroacetophenone obtained reached 37.5%. In production at present, as

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[illegible] the conditions governing the [illegible] [illegible] of [illegible] in [illegible] [illegible] the rate of yield has not reached this level.

2. Among improvements in the yield rates of various stages, the outstanding one is the process of extraction which is above 80%, so that the total yield rate for chloromycetin according to the calculation of [illegible] has reached 25 - 30%.

3. Research on aureomycin began in 1952. Due to the close cooperation of the research units in the Academy of Science, the Ministry of Light Industry, and the Ministry of Health, growth and purification phases of the antibiotic have met with preliminary success. Since the first part of 1955 experimental manufacture of it has been initiated. At present fermentation units are held steadily at more than 1,000, and the purification yield rate is stabilized at around 60%.

4. Research on streptomycin is progressing actively. At present molds to resist bacteriotropin have been found, and partial results have been obtained with the ion exchange agent used in the purification process.

In industrial production and research on experimental manufacture, we have concentrated chiefly on the above mentioned commonly used antibiotics.

## II. DEVELOPMENT OF THE ANTIBIOTIC INDUSTRY

Now permit me to review the development of China's antibiotic industry and the reason that it could develop. The accomplishment of scientific research in this is quite great. This must be discussed in several points.

1. In view of the need for it by the people, the party and the government recognized the importance of antibiotic research and its production. Furthermore it gave it great encouragement and support. During the period of the War of Resistance against Japan, medical personnel in a certain section of the People's Liberation Army (the Eighth Route Army at the time) used the culture broth for penicillin in bandaging the wounded in the area of the Tai-hsing Mountains. After the liberation, research activities developed rapidly. Units under the Ministry of Health and certain institutes in the Academy of Science had their personnel and facilities increased to enlarge the scope of research items. Establishment of a National Antibiotic Committee strengthened the leadership for research. Many research results have been applied toward the production of penicillin. Other research efforts opened the way for production of chloramphenicol, aureomycin and streptomycin. In 1950 the Ministry of Health of the Central People's Government established the Central Bureau for Inspection of Biological Products which inspected antibiotics regularly, having thus a great effect on the supervision of their production. All of this is said to substantiate the fact that only under the great concern and true leadership of the Communist Party and the People's Government can the antibiotic industry have the accomplishments and development of the present.

2. The spirit of research and cooperation in the scientific worker are important factors in the development of the antibiotic industry. Rich rewards are reaped from research activites. Let me just mention what I know personally. Research on penicillin began quite early. During the War of Resistance against Japan, there were intellectuals in the nation who did pioneering research in the antibiotics on their own by growing penicillium notatum or observing its

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morphology and such. Mr. T'ang Fei-fan of the National Antibiotic Committee who is among us today found the mold of penicillium notatum in Kunming before the liberation in 1944, and he was able to produce penicillin by the surface growth method. Between 1946 and 1948 scientists at the former Office of Preventive Medicine at the Alter of Heaven (Tien-t'an) conducted research experiments on fermentation factors and fermentation media related to the submerged growth method and the method of purification. At the same time they also trained some personnel. However under the rule of the reactionary government in the past scientific research did not receive any attention nor support. After the liberation everything was different. In 1949, the year that the Chinese People's Republic was formed, research activities on penicillin was reorganized. Through the cooperative efforts of the Central Institute of Research on Biological Products of the Ministry of Health, the Shanghai Pharmaceutical Research Institute of the Chinese Academy of Science, the former Shanghai Penicillin Testing Institute which is now the Third Pharmaceutical Plant (Shanghai), research on fermentation methods was intensified, and explorations into methods of purification and crystallization were actively pursued. These activities established the first foundation for penicillin production. Research on chloramphenicol was carried out in 1950 by the Dairen Scientific Research Institute and the Shanghai Pharmaceutical Research Institute, both of the Chinese Academy of Science where problems relating to media and methods of production were solved. These have been applied toward the production of synthomycin. Research workers in the Institute of Pharmaceutical Research of the Chinese Academy of Science and the Laboratory of Industrial Pharmaceuticals of the Bureau of Industrial Pharmaceuticals of the Ministry of Light Industry are continuing their efforts toward a more economic method to isolate and convert the differently constructed optically active bodies in the manufacture of chloramphenicol with certain results. In 1953, under the leadership of the Committee on Antibiotics, scientists were organized to visit the factories in person, so that research and production of penicillin could really be coordinated. The same year research on streptomycin was initiated, and much work has been done on the improvement of microbial strains, fermentation, purification, and crystallization. Units participating in the research include the Chinese Academy of Science, a certain medical college, the Central Institute of Research on Biological Products of the Ministry of Health, the Shanghai Industrial Laboratory of the Ministry of Light Industry, the Third Pharmaceutical Plant (Shanghai) etc. Research on aureomycin which was initiated at the same time soon met with preliminary success in the selection and culture of microbial strains, and in fermentation and purification. (The cooperating units are the same as those aforementioned.) The Academy of Science also went into research on the physiological and chemical structure of the aureomycin producing mold. Efforts in the search for new antibiotic molds and substances have been initiated and certain molds with original bacterial capacity to resist certain diseases have been found. Then there is much work done with many results obtained by other research agencies and certain schools of higher learning in their research and the training of qualified workers. Furthermore much research has also been done in the field of inspection and regulation. Under the leadership of the party and the government, the scientists have overcome all kinds of research difficulties, in order to offer valuable material for the industrial production of antibiotics

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3. The diligence of the working masses created the conditions for the development of the antibiotics industry. When experimental manufacture of penicillin was begun in 1949, the Third Pharmaceutical Plant (Shanghai) of the Ministry of Light Industry was remodeled from an old automobile repair factory. Difficulties such as the lack of proper materials and facilities and technical problems were overcome. The workers made their own fermentation tanks, repaired all kinds of equipment, and explored many new methods. For example, a worker, comrade Ch'eng Ch'e (who has since been promoted to the position of vice-chief of the fermentation section), suggested revamping the valves used to introduce air pressure to reduce the fermentation and culture rate. Comrade Chu Chi-fu, a mechanic of the Biochemical Pharmaceutical Laboratory had the packaging machinery changed in 1954 so that the output per minute has been increased from 20 tubes to 38 tubes at the present time, which is practically a 100% increase in the production rate. Comrade Tsou Tsu-hao sent from the Planning Section of the North China Pharmaceutical Plant to intern at the Biochemical Pharmaceutical Laboratory has suggested the method of using silk to filter the emulsions so that large particles and black specks could be removed before bottling which is an application toward improving the quality of the product. As for the experimental manufacture of chloramphenicol, it was initiated in the research laboratory of the Northeast Pharmaceutical Plant in 1952. During this period comrade Ch'eng Chia-hsiang [illegible] solved the problem of using native sources as materials [illegible] production. From the manufacture of nitrobenzene, a new method [illegible] manufacture p-nitroacetophenone, so that chloramphenicol [illegible] produced in large quantities. Under [illegible] there are even better factors for its realization. The early period [illegible] experimental manufacture took place at the time when American imperialism was waging bacterial warfare on us. Comrades who participated in this experiment were so moved by their patriotism to defend China, resist the US, and aid Korea that for a time they continued their work through Sundays without stopping for rest. Difficulties in the beginning were many as both experience and available equipment was lacking. However, through the diligent efforts of the whole staff of workers, this experimental manufacture project began to reap results after a short while. During the last few years many qualified persons were also trained. However, speaking from the point of industrial production, this was only the beginning.

4. The aid given by international friends had a stimulating effect on China's antibiotic production techniques. The Soviet expert Koma Yasilev [sic] gave important suggestions to the Third Pharmaceutical Plant (Shanghai) regarding the manufacture of penicillin. He suggested (1) Shortening the fermentation period, and (2) using the counter current method of extraction. In time these have been put to application and have effected a change in increased production (production increased by about 33%). He also pushed the establishment of a working schedule, so that the managerial aspect of production could be properly developed. The study and application of the relationship between the growth morphology of penicillium notatum and its production strength was also suggested by specialist Yasilev so that the methods of production of penicillin could be even more scientific. As for antibiotic research he suggested the establishment of an Antibiotics Committee in 1952, to lead and encourage "creative cooperation," so that we could place emphasis on the thinking of comrades engaged in a united research effort, which in turn had a great effect on research. Soviet specialist Comrade Fedor Chassnov [sic] also directed and helped the Northeast

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Pharmaceutical Plant in the experimental manufacture of synthomycin. Besides these, specialists from Poland and Major General Sokar [sic] of India also gave us constructive ideas and practical help. The International Conference on Antibiotics that was held in Warsaw the first part of this year and the technical cooperation between nations gave great stimulation and much technical revelation to China's antibiotic industry and antibiotic research.

### III. PROBLEMS EXISTENT IN EXPERIMENTAL MANUFACTURE AND PRODUCTION AND DEMANDS ON SCIENTIFIC RESEARCH LISTED

#### 1. Penicillin

(1) Fluctuations in the amount produced shows that from the aspects of fermentation units and yield rates;

A. The fermentation units keep increasing each year, but the degree of fluctuation is quite high. The averages for the lowest month and the highest month in 1954 were 1,396 and 1,908 units per mlit. Among the 3,000 gallon cans, they were 1,112 and 2,133 units per mlit.

Comparative Chart of Monthly Averages in Production of Penicillin Fermentation Units (from 1954 to 1955)

| Container type | Year and month | Jan | Feb | Mar | Apr | May | Jun |
|---|---|---|---|---|---|---|---|
| 1500 gallon container | 1954 | 1423 | 1396 | 1440 | 1462 | 1731 | 1542 |
| | 1955 | 1611 | 1489 | 1828 | 1858 | 1725 | 1864 |
| 3000 gallon container | 1955 | 1129 | 1112 | 1504 | 1605 | 1671 | 1640 |

| Container type | Year and month | Jul | Aug | Sep | Oct | Nov | Dec |
|---|---|---|---|---|---|---|---|
| 1500 gallon container | 1954 | 1503 | 1434 | 1504 | 1598 | 1839 | 1908 |
| | 1955 | 1792 | 1663 | 1979 | 2232 | | |
| 3000 gallon container | 1955 | 1770 | 1603 | 1711 | 2138 | | |

The causes for fluctuation are many. For instance, when mold strains from batch number 22 ching mark were used in December 1954, and mold strains from batch number 5_-20 were used in February 1955, the fermentation units were increased which affirmed the fact that mold strains were involved. Then in September 1954, when new cottonseed meal was used, and in March 1955, when a 2% peanut meal cake was used to complement cottonseed meal, it was found that the fermentation units also increased, which affirmed the involvement of media and their sources. Since the 3,000 gallon containers have been put into production use this year, the level of fermentation units possible through their use have been increasing gradually toward the level possible through the use of the 1,500 gallon containers. This proves to be the result of better agitation and aeration through revision of [illegible] in July. [illegible] of equipment and facilities. [illegible] ... of temperature, aeration, the addition of oil, through sterilization, the complete [illegible] of media and other materials all affect the [illegible] of fermentation while these factors cannot be [illegible] as they interact and many aspects are affected. In experimental manufacture and production, we cannot analyze the whole picture from [illegible] posed by these factors. As we still hold a definite [illegible] toward the study of the various factors, it fully shows that we have not mastered the law of fermentation. The result is we cannot actively control the stabilization of high fermentation unit production and its continual increase. However it is not hard to see that the key problem is a thorough understanding of the physiological and biochemical qualities of the mold strains, the raw materials used in production, and the interrelated steps in the use of equipment such as aeration and agitation which will be the answer. I figure the same or similar problems will be found in the experimental manufacture and production of streptomycin and aureomycin. Furthermore these vital problems must be solved through basic research.

Mold culture incidents continue to happen during the penicillin fermentation process. The culture rate in 1952 was 5.78%, in 1953 4.63%, in 1954 3.09%, and up till October 1955 it was only 3.78%. Factors governing the culture of microbial organisms are still undetermined.

B. The yield rate through extraction and purification continues to increase each year. In 1954 it averaged 66.19%, and in 1955 (up till October) it was 73.60%. However, fluctuations were quite obvious. For example the yield rate from the 1,500 gallon containers reached a peak in September with 86.92%, but it had been as low as 55.57%. In order to stabilize the yield rate at a comparatively high level, while constantly trying to raise it, research must be conducted on methods of purification and the chemical and chemical engineering aspects of facilities and equipment to control it.

(2) Problems still exist in the quality of the product. They are found in the strength of penicillin G and oil suspensions of penicillin.

A. The strength of penicillin G: In the temporary requirements governing the certification of antibiotics established by the Ministry of Health in 1954, the standard for procaine penicillin is 950 units purity per mg and the strength of penicillin G must be above 855 units per mg. Samples taken at random from products manufactured by the Third Pharmaceutical Plant (Shanghai) of the Ministry of Light Industry to the Central Bureau for Inspection of Biological Products showed fluctuations in purity and the strength of penicillin G. Some samples were substandard. Therefore efforts hereafter should be directed toward discovering the fundamental law to stabilize the strength and purity of penicillin G through further study of mold behavior and fermentation methods.

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B. Oil suspensions of procaine penicillin. Since manufacture of oil suspensions of penicillin was begun during the fourth period of 1951, it was found that there were disadvantages to its compounding by the freezing method which resulted in the separation of layers in the suspension. The suspension was difficult to draw into the syringe and there was local reaction after injection. In October 1954 compounding was changed to the heating method and the grinding period was also lengthened which resulted in a change for the better. However the size of the crystals still were not sufficiently small to meet the standards set down by the temporary requirements governing the certification of antibiotics, which meant that any crystal under 5 mm will meet 65% of the requirement. However it cannot be guaranteed that the largest crystal will be under 50 mm in size. It is hoped that research efforts on methods of crystallization will be intensified to basically solve the problem of insufficient minuteness of crystal size which is substandard.

C. Another important problem which is related to the quality of the product is the lack of unity in the methods and results of analytical assay and inspection among the different agencies and pharmaceutical concerns. For example drug effectiveness tested by the Third Pharmaceutical Plant is higher than that done by the Central Bureau for Inspection of Biological Products and also that by the Biochemical Pharmaceutical Laboratory. There were also differences in the results of the bactericidal and bacteriostatic qualities of the drug. Since analytical assay is the basic factor in quality assurance, it is hoped that after systematic and scientific study a definite basis could be found to standardize methods of analytical assay. In the process of production assay methods for the standardization and control of intermediate products have not been completely set up, which have resulted in obstacles to improvements in technique and management. This is a problem deserving study.

(3) There are also problems in the standardization of raw materials and their methods of application.

As for raw materials, the proportion of lactose used in relation to cost is quite great. According to statistics made the their period of 1955, the cost of lactose is more than 1/3 of total cost spent on all raw materials. Furthermore lactose is expensive and it is not easily supplied in large amounts at the present time. For industrial purposes research must find a satisfactory substitute. According to Wen Hsien [Literary Offerings] and the result of experiment by the Central Institute of Research on Biological Products, using cornmeal to replace most of the lactose could produce the same amount of units, except that a longer fermentation period was required. It is obvious that a substitute for lactose can be found. Improvements in working techniques to shorten the fermentation cycle is also possible, except that a further step in research is needed.

Raw materials such as cottonseed cakes and peanut cakes are agricultural products which are comparatively cheaper and easier to supply. However, due to such factors as plant strains and the season and methods of application, there are often great differences in their composition. Their composition must be standardized, and they must be used in the right ratio. It must be understood that with the problem of raw materials, substitute products and its use ratio are closely related to the physiology of the mold. Only thorough research and a complete set of scientific figures can solve it. Otherwise production is blind and to talk about a technical



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[illegible] and economic planning to [illegible] basis. It is hoped that a systematic study could be done on this problem to produce a conclusion.

2. Aureomycin and Streptomycin

(1) Aureomycin is in the process of being manufactured on an experimental basis, and samples are already available for clinical use. However there are still many existing problems.

A. From the standpoint of fermentation. Since adoption of mold strain K1001, unit production has been increased to an average of 1,300 units per mlit in the 63 gallon containers. However the fermentation units averaged from the 200 gallon containers is comparatively lower. As for raw materials used in fermentation, a substitute has not yet been found for the protein used in the culture medium which is very expensive. Laws regarding mold "take" and spore inoculation, factors related to fermentation, such as the utilization rate of air, have not yet been found.

B. Method of isolation originally used precipitation with calcium salts. There are still difficulties in the filtering process and condensing by vacuum. The yield rate is only 60%, and the steps are comparatively numerous (7 steps). It is hoped that comparative studies will be done on the extraction of filtrate solution.

(2) Study of streptomycin is being carried out in the different industrial agencies, but many problems still remain unsolved.

A. A bacteriotropin resistant strain has been cultivated, but its resistance is not strong enough, nor is it stable enough. Even with stimulation by ultraviolet rays its capacity to produce streptomycin does not seem to be increased. Its fermentation units range between 500 units to 600 units, and an understanding of its characteristics is yet to be obtained. Control of the fermentation process is not easy. These combined conditions result in the absence of a superior microbial strain being cultivated. Until then fermentation cannot be expanded. The urgent problems requiring attention are cultivation of microbial strains and prevention of bacteriotropin.

B. Filtering difficulties in the extraction process have been solved. The yield rate of crude sulfates extracted with an ion exchange agent ranges from 50% to 60%. The yield rate of the crystalline double salt with calcium chloride purified from the crude product is 40%. Further research must be done on increasing the yield rate, on the ion exchange agent and its sources.

In brief, many practical problems need to be solved in the production of aureomycin, while problems requiring basic research for a solution to the production of streptomycin are even greater in number.

3. Synthomycin

From the standpoint of production and development at present, production techniques of synthomycin are still faced with the following problems.

(1) Due to a longer period required for its synthesis, fluctuations of the yield rate in the various stages of production are quite obvious. As a reliable method to control and to analyze the many intermediate bodies is yet to be found, simply determining the

ultimat[illegible] point will not solve the problem. For example, the melting point of the reduced synthetized product and the yield rate of reduction do not seem to have any obviously close connection. Another example is seen in the 5 steps taken from the introduction of bromine to reduced synthesis which is a continuous process whereby the intermediate bodies do not undergo dry separation, nor are the contents analyzed. Calculation of the amount of ingredients used can only be drawn from an average estimate. Under conditions where there is so much fluctuation in the yield rate, loopholes in production can arise with that much more ease.

(2) Since production has been initiated, the degree of yield rate fluctuation in the step of reduction has been great and further stucy is needed to stabilize it. When reduction is not effective, then byproducts which do not dissolve in acid often appear during the next step of hydrolysis which will lower the yield rate. At present there is no hunch to ward off the appearance of these by-products.

(3) During the oxidation of nitrobenzene, air or oxygen is used as the oxygen source to produce the catalytic reaction which need further study and development at the present time. This involves many aspects, such as the production of free bases, production, and breaking down of peroxides which are problems related to theoretical organic chemistry.

(4) Toward the end of the distillation period, nitrosobenzene often heats up, resolves, and lets off nitrous gas in which lies the danger of explosion. At present there is no definite way to avoid such danger. Recently, a type of polynitrophenyl has been separated from nitrosobenzene which may be one of the causes responsible for this phenomenon, but it has not been determined that this is the only cause.

(5) A method to separate the optically active bodies which is suitable for industrial production still need further research and development. It is to be expected that the problem of disintegration of the dextro rotating bodies will be solved at the same time.

(6) As synthomycin which is often used in the different types of childhood dysentery, is extremely bitter in taste, there is an urgent need to develop a tasteless synthomycin. The quantity of its dosage is also rather big. A convenient quantity supplying sufficient is also a big problem needing our attention.

(7) Materials used in the production of synthomycin, such as hydrochloric acid and bromide, are strong corrosives which present a serious problem in the corrosion of equipment at present. Using only glass equipment still does not solve all the problems. Therefore it is especially important that this problem related to acid resistant materials is presented for your attention and advice.

From the problems listed above it can be seen that many aspects of production techniques are unfamiliar and not clear. Especially when production goes on continuously, the requirements are higher each day, and the problems involve many related aspects of basic research. To use the regular production of penicillin as an example, the many chains in its production, such as the nature of the microbial strain, the method of production, the manufactured dosage all have problems which require further research. At present, control of the nature of the microbial strains used in the production of penicillin, streptomycin, aureomycin from the standpoint of physiology and biochemistry is inadequate. The result of this finds the involved problems of culture media and fermentation factors still unsolved, and the whole picture is one of passivity. Some people feel that in our work of antibiotic research and production and the accomplishments of microbiology have fallen behind the needs of reality. We also have the same feeling, as this is one of the key problems industrial production asks scientific research to solve. Its purpose is the guarantee of production stability and production increase, which is effectively controlled from an active position. Then in the field of chemistry and industrial chemistry, some methods of extraction and purification are quite crude, and other methods have yet to be established. Therefore to coordinate production and the development of production, the problems that need to be studied are many, and they are problems requiring urgent attention. Originally antibiotic products are produced to meet the health needs of the great masses of people. Therefore in order for us to produce antibiotics that are low priced, of high quality, and clinically effective, the wholehearted cooperation of the research scientist is needed to fulfill this glorious task together. In conducting research the practical conditions of China should be coordinated into it, and problems should be considered with present industrial factors in mind and with the urgency of their development in the future. For example at present there is much work to be done on the selection of raw materials. Research on the application of cottonseed meal and peanut cake instead of the cornmeal that China has yet to produce in great amounts has shown certain results. This is good, but ehter is a need for further systematic research. Research on culture media for streptomycin and aureomycin is worth a trial in this direction. Equipment and apparatus can also be objects for further study.

China is a great nation with 600 million people, which will need all types of antibiotics in great amounts. Research related to antibiotics, and the equipment to produce antibiotics need thoroughly skilled personnel to handle it. Therefore a planned program to train skilled workers is worthy of everybody's attention.

Due to the concern by the Chinese Communist Party and the People's Government over the health of the whole nation, our antibiotics industry has had a very good start since the liberation, but it is far from sufficient to meet the health needs of the great masses of people. China's First Five-Year Plan has shown us the direction and we know this task to be difficult and glorious at the same time. Industry has great expectations of scientific research work, for it is only after research has had results that industrial production can progress another step. We firmly believe that on the basis of continuous results of scientific research, we can fulfill the task assigned us by the First Five-Year Plan and further create conditions for enlarging industrial production of antibiotics.

Now let me express my confidence in the success of this conference, and wish you all good health.

1 October 1955

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